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JOHN P WHITE
COOPER & DUNHAM LLP
1185 AVENUE OF THE AMERICAS
NEW YORK, NY 10036

EXAMINER	
GOLDBERG, JEANINE ANNE	
ART UNIT	PAPER NUMBER
1634	21

DATE MAILED: 03/27/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/327,750	SATO, TAKA-AKI	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,8-23,29,55,56 and 131-133* is/are pending in the application.

4a) Of the above claim(s) *29, 55-56, 131, 133* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,8-23 and 132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,10* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *21* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I in Paper No. 20 is acknowledged. The response traverses the restriction. Applicant's election with traverse of Group I in Paper No. 20 is acknowledged. The traversal is on the ground(s) that restriction is only required when the inventions are independent and distinct. This is not found persuasive because dependent inventions may be properly restricted if they are distinct. As discussed in MPEP 803, one of the two criteria for requirement of restriction is that the "inventions must be independent (see MPEP 802.01, 806.04, 808.01) or distinct as claimed". Accordingly, the demonstration of distinctness of the inventions is sufficient grounds for restriction. As stated in MPEP 802.01 "(t)he law has long been established that dependent inventions (frequently termed related inventions) such as those used for illustration above may be properly divided if they are, in fact "distinct" inventions, even though dependent". Applicants further argue that it would not be an undue burden to examine the claims of all groups I-V. However, it is maintained that undue burden would be required to examine the claims of groups II, III, IV and V along with the claims of group I as evidenced by the fact that the claims of groups I and (II, III, IV and V) have acquired a separate status in the art as recognized by their different classification and as recognized by their divergent subject matter and because a search of the subject matter of invention 1 is not co-extensive with a search of inventions II-V.

The requirement is still deemed proper and is therefore made FINAL.

New Matter

2. The amendments filed January 29, 2001, April 23, 2001, June 18, 2001, October 15, 2001 are objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. The specification failed to contain a sequence listing and a computer readable format on disk. The response to the notice to comply is not consistent with the originally filed specification. For example, SEQ ID NO: 28 appears to be the sequence found in Figure 1G-1 (mouse). The sequence provided in the computer readable format differs by 4 nucleotides from the nucleic acid originally filed. For example, position 237 of the figure is g whereas position 237 of the sequence listing is c. Similarly, position 342, 604 and 652. The sequence found in SEQ ID NO: 28 does not appear to be supported in the originally filed specification. Moreover, SEQ ID NO: 29 contains different nucleotides. Position 871 is a "t" in Figure 1G-2, but is a "c" in the SEQ ID NO: 29. The examiner has not compared the figures to each of the 45 SEQ ID NO: provided in the sequence listing. Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112- Enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-4, 8-23, 132 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of using known proteins which bind to p75NTR, does not reasonably provide enablement for NADE molecules of Figures 1G-1 and 1G-2 disclosed in the instant specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The claims are drawn to any isolated nucleic acid molecule encoding a polypeptide capable of binding with a p75NTR receptor.

The specification teaches nucleic acid sequence of 1G-1 and 1G-2 which the specification teaches are NADE nucleic acid molecules. The specification teaches p75NTR is a low-affinity neutrophin receptor that can mediate cell survival or cell death by NGF or another neutrotphin. The specification teaches that NADE specifically binds to p75NTRICD as a target. NADE has a significant homology to human HGR74 (page 1, lines 29-30). NADE mRNA is expressed the highest in the brain, heart and lung (page 1, lines 33-35).

The art teaches numerous nucleic acid sequences which encode amino acid sequences which are either 100% identical to an amino acid encoding SEQ ID NO: 12 or 13 or have very high homology to SEQ ID NO: 12 or 13 which would have the capability to bind with a p75NTR receptor. Each of these teachings in the art, however, is silent with respect to a specific, substantial utility. The art (Khursigara et al. J. of Biol. Chem. Vol 274, No. 5, pages 2597-2600, 1999) teaches the p75 receptor binds with TRAF6, NGF, BDNF, NT-3 and NT-4/5 (page 2598). The NGF gene has been cloned,

purified, characterized (Iwane et al. Biochem. Biophys. Res. Comm. Vol 171, No. 1, pages 116-122, August 1990). The art also teaches the induction of apoptosis by p75 neurotrophin receptor in human neuroblastoma cells (Bunone et al. Oncogene, Vol 14, pages 1463-1470, 1997 (Exhibit 4-1/3/00)). Bunone teaches that p75NTR could activate the cell death program by itself (abstract).

The specification does not appear to teach a specific and substantial use for the nucleic acids encoding NADE of Figure 1G-1 and 1G-2. While the specification appears to provide a working example directed to co-expression of NADE and p75NTR inducing apoptosis, this does not appear to be a real world use for a skilled artisan. The art however teaches that p75NTR alone may induce apoptosis. Therefore, the co-expression of p75NTR with NADE is not surprising and does not provide the skilled artisan how to use the NADE protein. The specification teaches that the protein may be administered to subjects in amounts effective to induce apoptosis (page 43). The specification however fails to enable this method, since the specification appears to purport that the co-expression of p75NTR and NADE induce apoptosis. The specification has not demonstrated any effective amounts to illustrate that in vivo administration leads to apoptosis induction. The skilled artisan would be required to perform undue experimentation to determine the effective amount and determine the extent of apoptosis.

Claim Rejections - 35 USC § 112-Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-4, 8-23, 132 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to any isolated nucleic acid molecule encoding a polypeptide capable of binding with a p75NTR receptor.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention". In analyzing whether

the written description requirement is met for a genus claim, it is first determined whether a representative number of species have been described by their complete structure.

The description in the specification as filed is not sufficient to convey that the applicant was, as of the filing date, in possession of the invention in a manner commensurate in scope with the claims. There is disclosed only a limited number of species, and applicants attempt to claim, on the basis of that single species, any nucleic acid capable of binding with a p75NTR.

Given this broad definition, the scope of the claims would appear to be much broader than the particularly disclosed species, and one is unable to envision, and the specification does not adequately describe, a commensurate number of species.

With the exception of the sequence within Figure 1G-1; 1G-2, and nucleic acid encoding proteins disclosed, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The nucleic acid itself is required. See *Fiers v. Fevel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be

unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

The specification teaches one gene sequence which binds with p75NTR. This single sequence is not representative of all sequences which are capable of binding with p75NTR. The art (Khursigara et al. J. of Biol. Chem. Vol 274, No. 5, pages 2597-2600, 1999) teaches the p75 receptor binds with TRAF6, NGF, BDNF, NT-3 and NT-4/5 (page 2598).

The specification teaches that alternative splice variants are likely (page 54). The specification has not described any isolated nucleic acid molecules which are splice variants which still bind to p75NTR. The description of these splice variants is further not provided.

The specification has described human, mouse, and rat molecules which have been deemed NADE. These three species within the broad genus of NADE molecules is not representative of the entire genus.

Therefore, only nucleic acids described in the specification in Figure 1G-1, 1G-2 and nucleic acids encoding disclosed proteins, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 112- Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 2-4, 12, 13, 15, 20, 23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2-4 lack proper antecedent basis. The claims are directed "the isolated DNA molecule", "the isolated cDNA molecule", and "the isolated RNA molecule". Claim 1 recited an isolated nucleic acid. Therefore, Claims 2-4 lack proper antecedent basis. This rejection may be easily overcome by re-writing the claims to recited, "The nucleic acid molecule of Claim 1, wherein the nucleic acid is DNA".

B) Claim 12 is indefinite because the claim appear to be directed to a nucleic acid which encodes the polypeptide shown in Figure 1G-1. Figure 1-G1 illustrates a nucleic acid. Therefore, it is unclear whether applicants have identified the incorrect figure or alternatively intended to claim the nucleic acid sequence of Figure 1-G1. As noted above, Figure 1-G1 does not appear to correspond to a sequence in the sequence listing.

C) Claim 13 does not appear to further limit Claim 3 and Claim 1. Claim 1 is directed to a nucleic acid molecule which encodes a polypeptide capable of binding p75NTR polypeptide.

D) Claim 15 does not include a SEQ ID NO: in the blank following SEQ ID NO:. As noted above, Figure 1-G1 does not appear to correspond to a sequence in the sequence listing.

E) Claim 20 and 23 contain the recitation "unique". It is unclear what encompassed by a unique sequence. The specification does not provide a definition of

unique. It is unclear whether the sequence must be found only within nucleic acids encoding NADE or whether the sequence is unique is some other means of base pairing or such.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. Claims 1-3, 8-11, 13-14, 16-21, 23, 132 are rejected under 35 U.S.C. 102(a) as being anticipated by Iwane et al. (Biochem. Biophys. Res. Comm. Vol 171, No. 1, pages 116-122, August 1990).

Iwane et al. (herein referred to as Iwane) teaches the human NGF gene which was isolated from murine leukemia virus LTR in a plasmid having dihydrofolate reductase cDNA. The expression plasmid was introduced into CHO cells (limitations of Claims 16-17). Figure 1 illustrates the structure of the expression plasmid for hNGF gene (limitations of Claims 1-3, 8-11, 13-14). The transformed CHO cells were cultured under conditions permitting production of the polypeptide and the polypeptides was

purified (limitations of Claim 18-19). Therefore, Iwane teaches an isolated nucleic acid molecule capable of binding with p75NTR receptor.

7. Claims 1-3, 8-11, 13-14, 16-21, 23, 132 are rejected under 35 U.S.C. 102(a) as being anticipated by Khursigara et al. (J. Biol. Chem. Vol 274, No. 5, pages 2597-2600, January 1999).

Khursigara et al. (herein referred to as Khursigara) teaches association of the p75 neurotrophin receptor with TRA6. Khursigara teaches preparing a DN TRAF6 contruct by amplifying the TRAF domain and ligating into a vector. The cells were cultured and transfected (page 2598). Khursigara teaches that the p75 receptor binds with TRAF6, NGF, BDNF, NT-3 and NT-4/5 (pages 2598, col. 2). As seen in Figure 1, levels of expression of the cultured proteins was determined. Therefore, Khursigara teaches an isolated nucleic acid molecule capable of binding with p75NTR receptor.

8. Claims 1-4, 8-14, 16-17, 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al. (Genbank Accession Number W46041, May 23, 1996).

Marra et al. (herein referred to as Marra) teaches a mouse embryo cDNA clone similar to the HGR74 (human). The nucleic acid encodes a protein which is 100% similar to SEQ ID NO: 12 and is 98.4% identical to SEQ ID NO: 12. The nucleic acid is from a house mouse (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Since the specification teaches that SEQ ID NO: 12 is a NADE amino acid, and that NADE amino acids bind with p75NTR, a sequence which is 100% similar to SEQ ID NO: 12 will inherently also have this characteristic.

9. Claims 1-4, 8-14, 16-17, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Marra et al. (Genbank Accession Number AI118980, September 1998).

As noted above, the specification appears to contain new matter because the nucleic acid originally filed and the nucleic acids presented in the sequence listings are not the same. A search of SEQ ID NO:s which appear in the sequence listing was performed. A sequence search of the Figures was not performed. A sequence search against the nucleic acids in the Figures would have had greater similarity.

Marra et al. (herein referred to as Marra) teaches a mouse embryo cDNA clone similar to HGR74 (human). The nucleic acid has a local similarity of 99.1% with SEQ ID NO: 28. The nucleic acid is 89.7% identical over the entire length of the molecule. The nucleic acid is from a house mouse (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Since the specification teaches that SEQ ID NO: 28 is a NADE nucleic acid, and that NADE binds with p75NTR, a sequence which has more than 99.1% local similarity to SEQ ID NO: 28 will also have this characteristic.

10. Claims 1-4, 11-13, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Brown et al. (Genbank Accession Number AF097440, April 1999).

As noted above, the specification appears to contain new matter because the nucleic acid originally filed and the nucleic acids presented in the sequence listings are not the same. A search of SEQ ID NO:s which appear in the sequence listing was performed. A sequence search of the Figures was not performed. A sequence search against the nucleic acids in the Figures would have had greater similarity.

Brown et al. (herein referred to as Brown) teaches a mouse brain expressed X-linked protein 3 (Bex3) mRNA. The nucleic acid has a local similarity of 99.3% with SEQ ID NO: 28. The nucleic acid is 96.6% identical over the entire length of the molecule. The nucleic acid is from a house mouse (limitations of Claims 11, 14).

Since the specification teaches that SEQ ID NO: 28 is a NADE nucleic acid, and that NADE binds with p75NTR, a sequence which has more than 99.3% local similarity to SEQ ID NO: 28 will also have this characteristic.

11. Claims 1-4, 11-13, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Faria et al. (Genbank Accession Number AF051347, October 1998).

Faria et al. (herein referred to as Faria) teaches a mouse REX-3 mRNA, complete cds. The nucleic acid of Faria encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 30. The nucleic acid is from a house mouse (limitations of Claims 11, 14).

Since the specification teaches that SEQ ID NO: 30 is a mouse NADE nucleic acid, and that NADE binds with p75NTR, a sequence which 100% identical to SEQ ID NO: 30 will also have this characteristic.

12. Claims 1-4, 11-13, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Brown et al. (Genbank Accession Number AF097438, April 1999).

Brown et al. (herein referred to as Brown) teaches a mouse brain expressed X-linked protein 1 (Bex1) mRNA. The nucleic acid of Brown encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 30. The nucleic acid is from a house mouse (limitations of Claims 11, 14).

Since the specification teaches that SEQ ID NO: 30 is a mouse NADE nucleic acid, and that NADE binds with p75NTR, a sequence which 100% identical to SEQ ID NO: 30 will also have this characteristic.

13. Claims 1-4, 11-13, 20-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Rapp et al. (Genbank Accession Number M38188, March 1995).

As noted above, the specification appears to contain new matter because the nucleic acid originally filed and the nucleic acids presented in the sequence listings are not the same. A search of SEQ ID NO:s which appear in the sequence listing was performed. A sequence search of the Figures was not performed. A sequence search against the nucleic acids in the Figures would have had greater similarity.

Rapp et al. (herein referred to as Rapp) teaches a human unknown protein from clone pHGR74 mRNA, complete cds. The nucleic acid of Rapp encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 13. The nucleic acid is from a human (limitations of Claims 11, 14). The nucleic acid of Rapp is 99.8% identical with SEQ ID NO: 29 (100% identical with Figure 1G-2).

Since the specification teaches that SEQ ID NO: 13 is a human NADE amino acid, and that NADE binds with p75NTR, a nucleic acid sequence which encodes a protein which 100% identical to a sequence comprising SEQ ID NO: 13 will also have this characteristic.

14. Claims 1-4, 8-14, 16-17, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by NCI-CGAP et al. (Genbank Accession Number AA576958, September 1997).

NCI-CGAP teaches a human cDNA clone similar to HGR74 (human). The nucleic acid of NCI-CGAP encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 13. The nucleic acid is from a human (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Since the specification teaches that SEQ ID NO: 13 is a human NADE nucleic acid, and that NADE binds with p75NTR, a nucleic acid sequence which encodes a

protein which 100% identical to a protein comprising SEQ ID NO: 13 will also have this characteristic.

15. Claims 1-4, 8-14, 16-17, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Hillier et al. (Genbank Accession Number N34237, January 1996).

Hillier teaches a human cDNA clone similar to HGR74 (human). The nucleic acid of Hillier encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 13. The nucleic acid is from a human (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17). Since the specification teaches that SEQ ID NO: 13 is a human NADE nucleic acid, and that NADE binds with p75NTR, a nucleic acid sequence which encodes a protein which 100% identical to a protein comprising SEQ ID NO: 13 will also have this characteristic.

16. Claims 1-4, 11-13, 20-23 are rejected under 35 U.S.C. 102(a) as being anticipated by Lee et al. (Genbank Accession Number AI227867, January 1999).

Lee et al. (herein referred to as Lee) teaches a rat brain cDNA clone. The nucleic acid of Lee encodes a protein which is 99.153% identical with the amino acid comprising SEQ ID NO: 34. The nucleic acid is from a rat (limitations of Claims 11, 14).

Since the specification teaches that SEQ ID NO: 34 is a rat NADE nucleic acid, and that NADE binds with p75NTR, a sequence which 99.1% identical to SEQ ID NO: 34 will also have this characteristic.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. Claims 18-19, 132 are rejected under 35 U.S.C. 103(a) as being unpatentable over Marra et al. (Genbank Accession Number W46041, May 23, 1996); Marra et al. (Genbank Accession Number AI118980, September 1998); NCI-CGAP et al. (Genbank Accession Number AA576958, September 1997); Hillier et al. (Genbank Accession Number N34237, January 1996); in view of Sambrook (Molecular Cloning, A Laboratory Manual, 1989).

Marra et al. (herein referred to as Marra) teaches a mouse embryo cDNA clone similar to the HGR74 (human). The nucleic acid encodes a protein which is 100% similar to SEQ ID NO: 12 and is 98.4% identical to SEQ ID NO: 12. The nucleic acid is from a house mouse (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Marra et al. (herein referred to as Marra) teaches a mouse embryo cDNA clone similar to HGR74 (human). The nucleic acid has a local similarity of 99.1% with SEQ ID NO: 28. The nucleic acid is 89.7% identical over the entire length of the molecule. The nucleic acid is from a house mouse (limitations of Claims 11, 14). The nucleic acid has

been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

NCI-CGAP teaches a human cDNA clone similar to HGR74 (human). The nucleic acid of NCI-CGAP encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 13. The nucleic acid is from a human (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Hillier teaches a human cDNA clone similar to HGR74 (human). The nucleic acid of Hillier encodes a protein which is 100% identical with the amino acid comprising SEQ ID NO: 13. The nucleic acid is from a human (limitations of Claims 11, 14). The nucleic acid has been placed in a vector, pT7T3D-Pac (limitations of Claims 8-10). The vector was placed in a host cell, namely BH10B (limitations of Claims 16, 17).

Neither Marra, NCI-CGAP nor Hillier teaches producing the polypeptide following insertion into a vector and host cell.

However, Sambrook teaches methods for expressing large amount of protein from a cloned gene introduced into E.coli have proven invaluable in the purification, localization, and functional analysis of proteins (17.2). Sambrook teaches culturing the cells and screening transformants for colonies. Sambrook teaches quantitating the levels of expression of cloned genes (17.34).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have cultured the host cell of Marra, NCI-CGAP or Hillier for the express benefit

taught by Sambrook. Sambrook teaches "methods for expressing large amount of protein from a cloned gene introduced into E.coli have proven invaluable in the purification, localization, and functional analysis of proteins (17.2)". Therefore, the ordinary artisan would have recognized that expressing cloned genes is a efficient means of generating large amounts of protein which may be further analyzed.

Conclusion

18. No claims allowable.

19. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Pharmacia Biotech Molecular and Cell Biology Products Catalog 1994 (page 130). The structure of pT7T3D vector.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. The examiner can normally be reached Monday-Friday from 8:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of formal matters can be directed to the patent analyst, Chantae Dessau, whose telephone number is (703) 605-1237.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Jeanine Goldberg
March 25, 2002

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600